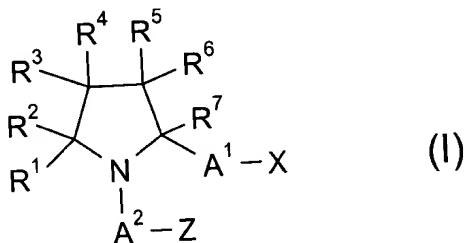


Please amend the above-captioned application as follows:

In the Claims

Please cancel claims 57 and 58. Please amend claims 31, 32 and 59 without prejudice or disclaimer as follows (clean text; a marked-up copy of the amended claims is attached as an Appendix hereto):

\ 31. (Twice Amended) A compound of formula (I)



wherein

R<sup>1</sup> to R<sup>7</sup> are independently selected from H, optionally substituted C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl and C<sub>2-6</sub> alkynyl, optionally substituted aryl, OH, halogen, CN, OR<sup>12</sup>, SR<sup>12</sup>, COR<sup>12</sup>, NR<sup>13</sup>R<sup>14</sup>, CONR<sup>13</sup>R<sup>14</sup>, SO<sub>2</sub>NR<sup>13</sup>R<sup>14</sup>, where R<sup>13</sup> and R<sup>14</sup> are COOR<sup>12</sup>, SOR<sup>12</sup>, SO<sub>2</sub>R<sup>12</sup>, and two of R<sup>1</sup> to R<sup>7</sup>, independently selected from H and C<sub>1-3</sub> alkyl and R<sup>12</sup> represents C<sub>1-6</sub> alkyl; together with the atoms connecting them, optionally form a 3- to 6-membered ring system; at least one of the pairs R<sup>1</sup> and R<sup>2</sup>; R<sup>3</sup> and R<sup>4</sup>; and R<sup>5</sup> and R<sup>6</sup> is optionally replaced by an optionally substituted alkylidene group or =O; and two of R<sup>1</sup> to R<sup>7</sup> which are positioned at adjacent carbon atoms are optionally replaced by a C-C bond;

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A<sup>1</sup> is selected from (-CR<sup>8</sup>R<sup>9</sup>-)<sub>n</sub>, optionally substituted C<sub>3-6</sub> cycloalkylene and a combination of these groups, R<sup>8</sup> and R<sup>9</sup> being independently selected from H, C<sub>1-6</sub> alkyl, halogen, OH, OR<sup>12</sup> and NR<sup>13</sup>R<sup>14</sup>, where for n ≥ 2, R<sup>8</sup> and R<sup>9</sup> are the same or different in each group and two groups selected from R<sup>8</sup> and R<sup>9</sup> at adjacent C atoms are optionally replaced by a C-C bond, and a group -O- or -CO- is optionally positioned between two adjacent groups CR<sup>8</sup>R<sup>9</sup>; and wherein one of R<sup>8</sup> and R<sup>9</sup> is optionally combined with one of R<sup>1</sup> to R<sup>7</sup> to form a 5- to 7-membered ring structure; and n = 1, 2, 3 or 4;

X is selected from COOM and groups which are capable of being converted into COOM under physiological conditions, M being selected from H and pharmaceutically acceptable cations;

A<sup>2</sup> is (-CR<sup>10</sup>R<sup>11</sup>-)<sub>m</sub>, where R<sup>10</sup> and R<sup>11</sup> are independently selected from H, C<sub>1-2</sub> alkyl and halogen; where for m ≥ 2 the groups R<sup>10</sup> and R<sup>11</sup> are the same or different in each group, a group -O- or -S- is optionally positioned between two adjacent groups -CR<sup>10</sup>R<sup>11</sup>-, and two groups selected from R<sup>10</sup> and R<sup>11</sup> at adjacent C atoms are optionally replaced by a C-C bond; and wherein one of R<sup>10</sup> and R<sup>11</sup> is optionally combined with one of R<sup>1</sup> to R<sup>9</sup> to form a 5- to 7-membered ring structure; and m is 1, 2, 3, or 4;

Z is selected from Y<sub>3</sub>C-O-, Y<sub>2</sub>C=CR<sup>15</sup>- and Y<sub>2</sub>C=N-O-, where R<sup>15</sup> is selected from H, C<sub>1-3</sub> alkyl or halogen and the groups Y are independently selected from optionally substituted C<sub>6-12</sub> aryl and optionally substituted C<sub>2-5</sub> heteroaryl having up to three heteroatoms

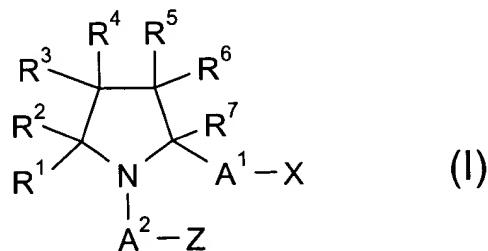
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independently selected from N, O and S, and the groups Y are optionally linked by a covalent bond or by groups between atoms belonging to different groups Y, said groups selected from -CH=CH-, -CH<sub>2</sub>- and -CH<sub>2</sub>CH<sub>2</sub>-;

and the individual stereoisomers of these compounds.

~~2~~ ~~32.~~ (Amended) The compound of claim ~~21~~, wherein R<sup>7</sup> is hydrogen and R<sup>1</sup> to R<sup>6</sup> are independently selected from hydrogen, optionally substituted C<sub>1-3</sub> alkyl, halogen, OH, CN, and optionally substituted phenyl.

~~21~~ ~~59.~~ (Twice Amended) A pharmaceutical composition comprising at least one of a pharmaceutically acceptable carrier and a pharmaceutically acceptable excipient and at least one compound of formula (I):



wherein

R<sup>1</sup> to R<sup>7</sup> are independently selected from H, optionally substituted C<sub>1-6</sub> alkyl, C<sub>2-6</sub>

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alkenyl and C<sub>2-6</sub> alkynyl, optionally substituted aryl, OH, halogen, CN, OR<sup>12</sup>, SR<sup>12</sup>, COR<sup>12</sup>, COOR<sup>12</sup>, SOR<sup>12</sup>, SO<sub>2</sub>R<sup>12</sup>, NR<sup>13</sup>R<sup>14</sup>, CONR<sup>13</sup>R<sup>14</sup>, SO<sub>2</sub>NR<sup>13</sup>R<sup>14</sup>, where R<sup>13</sup> and R<sup>14</sup> are independently selected from H and C<sub>1-3</sub> alkyl and R<sup>12</sup> represents C<sub>1-6</sub> alkyl; two of R<sup>1</sup> to R<sup>7</sup>, together with the atoms connecting them, optionally form a 3- to 6-membered ring system; at least one of the pairs R<sup>1</sup> and R<sup>2</sup>; R<sup>3</sup> and R<sup>4</sup>; and R<sup>5</sup> and R<sup>6</sup> is optionally replaced by an optionally substituted alkylidene group or =O; and two of R<sup>1</sup> to R<sup>7</sup> which are positioned at adjacent carbon atoms are optionally replaced by a C-C bond;

A<sup>1</sup> is selected from (-CR<sup>8</sup>R<sup>9</sup>-)<sub>n</sub>, optionally substituted C<sub>3-6</sub> cycloalkylene and a combination of these groups, R<sup>8</sup> and R<sup>9</sup> being independently selected from H, C<sub>1-6</sub> alkyl, halogen, OH, OR<sup>12</sup> and NR<sup>13</sup>R<sup>14</sup>, where for n ≥ 2, R<sup>8</sup> and R<sup>9</sup> are the same or different in each group and two groups selected from R<sup>8</sup> and R<sup>9</sup> at adjacent C atoms are optionally replaced by a C-C bond, and a group -O- or -CO- is optionally positioned between two adjacent groups CR<sup>8</sup>R<sup>9</sup>; and wherein one of R<sup>8</sup> and R<sup>9</sup> is optionally combined with one of R<sup>1</sup> to R<sup>7</sup> to form a 5- to 7-membered ring structure; and n = 1, 2, 3 or 4;

X is selected from COOM and groups which are capable of being converted into COOM under physiological conditions, M being selected from H and pharmaceutically acceptable cations;

A<sup>2</sup> is (-CR<sup>10</sup>R<sup>11</sup>-)<sub>m</sub>, where R<sup>10</sup> and R<sup>11</sup> are independently selected from H, C<sub>1-2</sub> alkyl and halogen; where for m ≥ 2 the groups R<sup>10</sup> and R<sup>11</sup> are the same or different in each group, a

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group -O- or -S- is optionally positioned between two adjacent groups -CR<sup>10</sup>R<sup>11</sup>-, and two groups selected from R<sup>10</sup> and R<sup>11</sup> at adjacent C atoms are optionally replaced by a C-C bond; and wherein one of R<sup>10</sup> and R<sup>11</sup> is optionally combined with one of R<sup>1</sup> to R<sup>9</sup> to form a 5- to 7-membered ring structure; and m is 1, 2, 3, or 4;

Z is selected from Y<sub>3</sub>C-O-, Y<sub>2</sub>C=CR<sup>15</sup>- and Y<sub>2</sub>C=N-O-, where R<sup>15</sup> is selected from H, C<sub>1-3</sub> alkyl or halogen and the groups Y are independently selected from optionally substituted C<sub>6-12</sub> aryl and optionally substituted C<sub>2-5</sub> heteroaryl having up to three heteroatoms independently selected from N, O and S, and the groups Y are optionally linked by a covalent bond or by groups between atoms belonging to different groups Y, said groups selected from -CH=CH-, -CH<sub>2</sub>- and -CH<sub>2</sub>CH<sub>2</sub>-.

#### **REMARKS**

The courtesy extended by Examiner Shameem to Applicants' representative during a personal interview on March 19, 2003 is acknowledged with appreciation. As discussed at the interview, reconsideration and withdrawal of the rejections made in the mentioned Office Action are respectfully requested, in view of the foregoing amendments and the following remarks.